

1997, has now been carefully studied. Reconsideration and allowance are hereby respectfully urged.

Briefly, the present invention relates to isolated DNA molecules which encode naturally occurring TBP-II. TBP-II is a novel tumor necrosis factor binding protein which is an extracellular domain of a TNF receptor. It was first disclosed in the parent applications of the parent application, and one claim directed to this protein was officially found to be allowable by the examiner in charge of the present case. The claims drawn to the protein in parent application of 07/930,443 are now involved in an interference proceeding with the claims of USP 5,344,915. The present application claims any isolated DNA molecule encoding the novel TBP-II protein, as well as replicable expression vehicles capable of expressing that protein, host cells transformed with such replicable expression vehicles and processes for producing the protein by culturing such host cells.

The interview between Examiner Schwadron and the undersigned attorney on October 4, 1997, is hereby gratefully acknowledged. In this interview, suggested amendments to the claims were discussed in order to obviate the 35 USC 112, first paragraph, rejection. Furthermore, the priority document was discussed and arguments were presented why the prior art rejections were not applicable. The arguments presented in the interview will be substantially repeated herein.

The examiner still considers that claims 14, 39, 42 and 45 are withdrawn from further consideration. However, it is noted that the examiner has indicated that in the event that the

claims currently under consideration are found allowable. The withdrawn claims will be treated as per MPEP §821.04. Claims 35 and 36 have been rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey that the inventors had possession of the claimed invention. The examiner states that there is no support in the specification as originally filed for the DNAs of claims 35 and 36. The examiner states that the specification discloses peptides containing the two aforementioned amino acid sequences but said peptides consist of 21 or 30 amino acids respectively. The examiner states that the peptides recited in the claims containing the aforementioned amino acids are peptides of 13 and 15 amino acids which are not disclosed in the specification. The examiner states that the recitation of the aforementioned peptides results in a DNA that is broader in scope than that disclosed in the specification in that it encompasses DNAs encoding peptides not disclosed in the specification such as the 13-or 15-mer in combination with amino acids not disclosed in the specification. This rejection is respectfully traversed.

The present claims have been amended to specify that they are directed only to DNA encoding a naturally occurring tumor necrosis factor. Thus, regardless of whether an N-terminal 13, 15, 21 or 30 amino acids are specified, it is the same DNA which is being covered. The claims are not being broadened or narrowed by truncating the N-terminal amino acid sequence as set forth in the specification.

The only reason why claims 35 and 36 present N-terminal amino acid sequences which are shorter than those disclosed at page 7 of the specification, for example, is because applicant wants to be certain that the claims are entitled to the effective filing date of the first Israeli priority application of May 18, 1989. At the time that the first priority application was filed, the sequence was effectively Xaa-Pro-Tyr-Ala-Pro-Glu-Pro-Gly-Ser-Thr ... . Thus, the N-terminus was only sequenced through the Gly-Ser-Thr residues. When the present application was filed, the N-terminal sequencing was completed somewhat further toward the C-terminus so as to include an additional 15 residues, as is disclosed on page 7 of the present specification, for example. However, it is the same protein which is being sequenced. An N-terminal sequence that ends with Gly-Ser-Thr identifies the same protein as the one defined by a longer N-terminal sequence. The shorter definition is being given in order to ensure that the claims are fully supported by the disclosure of applicant's priority application.

Accordingly, in view of the amendment to the claims to clarify that the claims are only drawn to DNA encoding the naturally occurring peptide and in view of the fact that the sequence ending only in Gly-Ser-Thr is fully supported by the priority application, it should be clear that the definition set forth in claims 35 and 36, which were selected so as to be fully supported by the priority application, is not broader than the disclosure and does not represent new matter or subject matter

which applicants did not invent. Reconsideration and withdrawal of this rejection are therefore respectfully urged.

Claims 11-13, 33-38, 40, 41, 43 and 44 have been rejected under 35 USC 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains to make and/or use the invention. The examiner states that the specification discloses a partial protein sequence and offers it up as enablement for nucleic acids encoding the isolated proteins and a broad range of other possible species. The examiner states that the claims encompass nucleic acids encoding innumerable muteins, variants and derivatives and that the claims under consideration are not drawn to DNA encoding a single protein. This part of the rejection is respectfully traversed.

Applicant has no intent to claim nucleic acids encoding the isolated proteins and a broad range of other possible species. Applicant only wishes to claim the DNA for a natural TBP-II substance. Natural TBP-II was first discovered by applicants. In order to clarify this intent, the claims have now been amended to specify that the DNA encodes "naturally occurring" TBP-II protein. In the interview, the examiner agreed that the addition of this language would avoid a substantial portion of the reason for objecting to the claims. Accordingly, it is urged that that part of the rejection which objects to the definition of the DNA merely by functional characteristics of the protein which it encodes has now been obviated.

The examiner cites the decision of In re Deuel, 34 USPQ2d 1210 (Fed. Cir. 1995) as stating that the disclosure of a partial protein sequence did not render obvious the DNA encoding the entire sequence. The examiner considers the situation here to be analogous in that applicants allege enablement of the claims and nucleic acids on the basis of the disclosure of a partial protein sequence without having taught any particular structure for the claims and nucleic acids themselves. This part of the rejection is respectfully traversed.

The Deuel decision was primarily directed toward the rejection of claims 5 and 7 of the Deuel application, which were specifically directed to the naturally occurring human or bovine cDNA encoding heparin-binding growth factor. The prior art disclosed a partial amino acid sequence of heparin-binding growth factor and methods for isolating the naturally occurring cDNA using probes based on that sequence. The court ruled, however, that the precise cDNA molecules of claims 5 and 7 would not have been obvious over the prior art because no claimed or closely related cDNA molecules were disclosed in the prior art and one could not have conceived of the subject matter of claims 5 and 7 because, until the claimed molecules were actually isolated and purified, it would have been highly unlikely for one of ordinary skill in the art to contemplate what was ultimately obtained. What cannot be contemplated or conceived cannot be obvious (34 USPQ2d at 1215).

The court ruled that the genetic code relationship did not overcome the deficiencies of the cited references because the prior art disclosure of the amino acid sequence of a protein

does not necessarily render particular DNA molecules encoding the protein obvious because the redundancy of the genetic code permits one to hypothesize an enormous number of DNA sequences coding for the protein and no particular one of these DNAs can be obvious unless there is something in the prior art to lead to the particular DNA and indicate that it should be prepared (34 USPQ2d at 1215).

The patent application involved in Deuel also included claims 4 and 6, which were of a different scope than claims 5 and 7. Claims 4 and 6, as with the claims of the present invention, generically encompass all DNA sequences encoding the protein in question. The court noted that such claims would probably have been obvious from the complete amino acid sequence of the protein coupled with the knowledge of the genetic code. However, because the primary reference only disclosed a partial amino acid sequence, the court also reversed the final rejection of claims 4 and 6, stating at 1216:

We will therefore also reverse the final rejection of claims 4 and 6 because neither the Board nor the patent examiner articulated any separate reasons for holding these claims unpatentable apart from the grounds discussed above.

Thus, it is clear that the obviousness of claims 4 and 6 from the partial amino acid sequence was never separately argued by the patent examiner or the Board, and therefore the court had no reason to specifically consider the very different issues which are involved for claims which generically encompass all DNA sequences encoding the protein in question. Thus, it can be said that Deuel contains a very strong holding that the

disclosure of a partial protein sequence does not render obvious the natural cDNA encoding that sequence, but the holding with respect to the generic DNA claims is much weaker in view of the fact that the parties did not separately argue these claims. If the arguments presented herein were before the court, then it is likely that a different conclusion would have been reached. In view of the fact that the issues were never argued before the court, Deuel should not be considered precedent for the present situation.

It is clear from Deuel, however, that if the prior art had disclosed the complete amino acid sequence, the DNA of the generic claims would have been considered to have been contemplated and conceived because the knowledge of the genetic code would have enabled a person of ordinary skill in the art to envision the idea of, and, perhaps with the aid of a computer, even identify all members of the claimed genus. Here, applicant was in physical possession of the novel protein in substantially purified form. It was sufficiently purified that a partial amino acid sequence could be obtained. The examiner has not argued that it would not have been within the skill of the art at the time the present invention was made to obtain the complete amino acid sequence of the protein without undue experimentation. This is not an issue of being unable to contemplate a single specific DNA sequence, as was the case with claims 5 and 7 of Deuel. Because a partial amino acid sequence is provided, a large part of the corresponding cDNA was also effectively provided in view of the genetic code. The rest of the protein sequence is inherent from the isolated protein which

was obtained by the present applicants. Therefore, the rest of the encoding DNA sequence was also inherently disclosed in the present disclosure. The examiner states that applicants have not taught any particular structure for the claimed nucleic acids themselves. However, the particular structure of the protein is inherently disclosed in the present specification. Since at least one claim to this protein has been found allowable in the parent case, it is apparent that the novel protein has been sufficiently described and enabled in the present specification. If the protein structure is sufficiently disclosed, either explicitly or inherently, then the nucleic acids which encode this protein by means of the genetic code are equally well disclosed.

The examiner states that there is no evidence of record that the intact DNA sequence of TBP-II can be obtained using the particular amino acid sequences disclosed in the specification without undue experimentation. However, applicant is not claiming the specific human cDNA encoding this protein. Applicant is generically claiming all DNA which encodes the protein, which has been substantially purified, partially sequenced and claimed in a manner found allowable in the parent case. It is not necessary to obtain the specific human cDNA in order to enable the present claims. They are enabled merely by the fact that the protein is enabled.

Furthermore, it is not understood why the examiner takes the position that the cDNA sequence of TBP-II could not be obtained using the particular amino acid sequence as disclosed in the specification without undue experimentation. Certainly,



prior to Deuel, examiners routinely made rejections on the ground that it would be obvious to obtain the human cDNA if the prior art was in possession of the partial amino acid sequence of the protein encoded by the cDNA. Indeed, this argument was strongly made by the examiner, Board and solicitor in the Deuel case and the court did not disagree. The court merely ruled that it did not matter whether a general method of isolating cDNA was known or obvious because this is essentially irrelevant to the question of whether the specific molecules themselves would have been obvious. Here, the claims are not directed to the specific cDNA molecule. However, the obvious method of obtaining the cDNA sequence for the purpose of confirming the entire amino acid sequence would have been obvious given the disclosure of the present specification for the same reason that the examiner considered it obvious to do so during the prosecution of In re Deuel and which was not refuted by the Deuel court. This is merely further evidence that those of ordinary skill in the art reading the present specification could obtain the entire amino acid sequence reading the present specification without undue experimentation. As long as the complete amino acid sequence could be obtained from the present specification without undue experimentation, the generic DNA sequences which encode that sequence by the genetic code are automatically contemplated for the same reason that a complete amino acid sequence in a prior art reference would have rendered a generic DNA claim obvious as stated by the Deuel court. Accordingly, this is another reason why the generic DNA sequence presently claimed was within the possession of the inventors at

the time the present application was filed and therefore fully complies with the first paragraph of 35 USC 112.

Reconsideration and withdrawal of this rejection are therefore respectfully urged.

With respect to the examiner's statement that there is no disclosure in the specification as to whether the particular amino acid sequences listed on page 23 are derived from the same molecule or that the molecule was found as four different but related molecules, the examiner's attention is invited to page 7, lines 10-11, where it states:

In fact, a heterogeneity of N-terminal sequences could be observed in the sample of TBP-II, . . . .

Thus, the present disclosure states that the different truncations of the sequence is due to a heterogeneity of N-terminal sequences. This means there is a single protein whose sequences merely have different truncations. The examiner has no reason to disbelieve this presumptively accurate statement in the present specification.

Claims 11-13, 33-38, 40, 41, 43 and 44 have been rejected under 35 USC 102(e) as being anticipated by Smith. The examiner states that Smith teaches the claimed inventions citing Figure 2A and the claims. The examiner states that the rejection can be overcome by the submission of English language copies of the foreign priority documents, assuming the claimed inventions are disclosed and set forth in priority documents. This rejection is respectfully traversed.

In the examiner's official action of December 9, 1996, the office action summary indicated that none of the certified

copies of the priority documents had been received. However, the examiner's attention is invited to paragraph 18 of applicant's transmittal letter for a new application under 37 C.F.R. §1.60 submitted on June 7, 1995, in this case. This paragraph informs the examiner that the benefit of the priority of three Israeli applications (90339, 91229, and 94039) were requested and stated that certified copies of each of said applications were filed in the parent case on May 16, 1990. It is respectfully requested that the examiner acknowledge receipt of the certified copies in the parent application. As the certified copies are in the English language, the examiner can readily determine that all of the present claims are indeed supported by the priority applications. Courtesy copies of the three priority applications were provided to the examiner at the interview. While these copies were not certified copies, the examiner can ascertain that the present claims are entitled to the effective filing date of the May 18, 1989, Israeli priority application, thereby antedating the Smith patent. The examiner need only go to the Interference Branch and compare the certified copy with the courtesy copy provided to the examiner to ascertain that they are identical so that the present rejection can be withdrawn. Reconsideration and withdrawal of this rejection are therefore respectfully urged.

Upon further consideration of the issues, applicant hereby withdraws its request for the institution of an interference proceeding with respect to patent 5,395,760. The present claims claim a genus of DNA molecules all encoding the TBP-II protein, while the claims of the Smith patent are

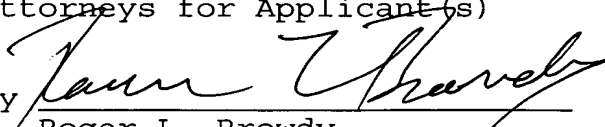
directed to the species of the natural cDNA. There is no interference-in-fact as the species would not be made obvious by the genus for the reasons enunciated by the Deuel court. Accordingly, while the present claims would dominate the claims of Smith, an interference would not be appropriate as the claims of Smith are patentably distinct from the present claims. It should be understood, however, that the above discussion is explicitly being made without prejudice toward applicant's ability to argue a different legal position if the examiner declares an interference despite applicant's withdrawal of a request therefor.

It is submitted that all of the claims now present in the case clearly define over the references of record. Reconsideration and allowance are therefore earnestly solicited.

Respectfully submitted,

BROWDY AND NEIMARK, P.L.L.C.  
Attorneys for Applicant(s)

By

  
Roger L. Browdy  
Registration No. 25,618

RLB:al  
419 Seventh Street, N.W.  
Washington, D.C. 20004  
Telephone No.: (202) 628-5197  
Facsimile No.: (202) 737-3528

roger\amd\wallac5b.amd